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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/905,508	08/04/97	SHAYESTEH	L 023070-0677

HM22/0616
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EXAMINER	
ARTHUR, L	
ART UNIT	**PAPER NUMBER**
1655	14

DATE MAILED: 06/16/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/905,508	Shayesteh et al.
Examiner	**Group Art Unit**
Lisa Athur	1655

☒ Responsive to communication(s) filed on *Mar 28, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *36-39* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *36-39* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *11*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. This application is a continuing prosecution application filed on March 28, 2000. Claims 1-22 have been canceled and claims 36-40 have been newly added and are the only pending claims.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 36,37,38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The essential feature of the claimed invention is the correlation between inhibition of PI kinase activity in cells and the resulting inhibition of proliferation of ovarian cancer cells in patients by administration of an inhibitor of PI kinase activity which more specifically is a non-peptidic inhibitor such as LY294002. The specification teaches that increased PI-kinase activity might contribute to tumor progression by increasing the rate of cell proliferation and tested this hypothesis by incubating cells from an ovarian cancer cell line with the known PI-kinase inhibitor LY294002. The specification teaches that this assay resulted in a significant decrease in cellular proliferation as measured by thymidine incorporation. This decreased proliferation rate was not

observed in cells which had normal PIK3CA copy number. The specification states that these studies suggest that therapeutic agents targeting the PI3-kinase pathway may be effective against ovarian cancers. However, the specification does not describe compounds other than LY294002 which inhibit PI-kinase activity such that a common structural feature of a PI-kinase inhibitory compounds was evident to the skilled artisan from the specification. The claims broadly encompass a potentially large genus of compounds which could inhibit PI-kinase activity, but the specification only describes one specific non-peptidic compound and fails to describe any of the structural feature of this compound which are responsible for its function in inhibiting PI-kinase to result in a decrease in cell proliferation of ovarian cells. The specification contains no description of how LY294002 interacts with Pi-kinase to inhibit its activity, such that the skilled artisan would know what other compounds having similar structure and/or function would be. The compounds which are encompassed by this genus of PI-kinase inhibitors appears to be diverse . Minaguchi et al. (CANCER RES. (1999)59:6063-6067) teach that the PTEN gene product encodes a phosphatidylinositol phosphatase which antagonizes the PI-kinase mediated pathway and suggests that overexpression of this gene product could be effective as a therapy for ovarian cancer by inhibiting PI-kinase activity. This inhibitor is structurally very different from that of LY294002 and the specification clearly did not describe such inhibits of PI-kinase. However, the inhibitor of Minaguchi et al. Would be encompassed by the claims as written. Consequently, absent a written description disclosing a representative number of species of the PI-kinase inhibitors which function to decrease cell proliferation of ovarian cells, the specification fails to

show that applicant was in fact, "in possession of the claimed invention" at the time the application was filed.

4. Claims 36-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not provide sufficient guidance and working examples to enable the skilled artisan to make and use the claimed method of inhibiting the pathological proliferation of ovarian cancer cells in a patient by inhibiting PI kinase activity in cells without undue experimentation. The specification teaches that increased PI-kinase activity might contribute to tumor progression by increasing the rate of cell proliferation and tested this hypothesis by incubating cells from an ovarian cancer cell line with the known PI-kinase inhibitor LY294002. The specification teaches that this assay resulted in a significant decrease in cellular proliferation as measured by thymidine incorporation. This decreased proliferation rate was not observed in cells which had normal PIK3CA copy number. The specification states that these studies suggest that therapeutic agents targeting the PI3-kinase pathway may be effective against ovarian cancers. However, the specification does not describe compounds other than LY294002 which inhibit PI-kinase activity, the specification provide any demonstration that the ability of LY294002 to decrease cell proliferation of an ovarian cancer cell line could be translated to the in vivo

environment in a patient. The specification provides no teaching that the in vitro results were known in the art to be predictable when extrapolated into the in vivo environment. Instead the specification states that therapeutic agents which target PI-kinase activity may be effective against ovarian cancer. Shayesteh et al. (Nature Genetics (Jan 1999) 21(1): 99-102.) teach that inhibitors of PI3-kinase will become interesting possible therapeutic agents against ovarian cancer when and if the model that increased PIK3CA copy number and the resulting increase in PI3-kinase activity increase cell proliferation and inhibit apoptosis to allow cells to survive and to genetically evolve into a more malignant phenotype, and if further studies show that PI3-kinase is activated in ovarian tumors as it seems to be in ovarian cancer cell lines. These teachings establish that extensive additional research is still required to determine whether or not inhibition of PI-kinase is a mechanism that will have an effect on cell proliferation in a patient and that the outcome is unpredictable due to the complexity of the mechanisms involved in cancers such as ovarian cancer and the difficulty in extrapolating in vitro results to the in vivo environment. Consequently, for the reasons set forth above, the skilled artisan would be required to practice undue experimentation to make and use the claimed treatment method.

5. No claims are allowable. However, the claims are allowable over the prior art because the prior art did not teach a method which correlated the inhibition of PI-kinase activity with decreased pathological proliferation of the ovarian cancer cells in the patient.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa Arthur whose telephone number is (703) 308-3988. The examiner can normally be reached on Monday-Wednesday from 7:00 am to 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1096.

Lisa B. Arthur

LISA B. ARTHUR
PRIMARY EXAMINER
GROUP 1800 1600

June 14, 2000